REMARKS

Claims 1 to 97 were pending in the present application. Claims 1 to 97 have been canceled without prejudice. Withdrawn claims 22-49, 52, 53, and 55-97, drawn to non-elected subject matter, thus have been canceled without prejudice. Applicants reserve the right to prosecute the subject matter of the canceled claims in one or more continuation, divisional, or continuation-in-part applications. New claims 98 to 113 are added. Claims 98-113 are believed to be within elected Group I. Applicants thank the Examiner for his willingness to examine the claims to the extent that they read on SEQ ID NO: 2, 28, 29, and 32. Support for new claims 98 to 113 can be found in the specification, *e.g.*, as set forth in the chart below.

Claims	Support
98	Page 9, line 36 to page 10, line 1; page 11, lines 11-16; page 12, lines 20-22; page 15, line 35 to page 16, line 4; page 29, line 35 to page 30, line 5; Figure 1B
99	Page 9, line 36 to page 10, line 1; page 11, lines 11-16; page 12, lines 20-22; page 15, line 35 to page 16, line 4; page 29, line 35 to page 30, line 5; Figure 1B; Figure 13
100	Page 10, line 2; page 11, lines 11-16; page 12, lines 24-28; page 15, line 35 to page 16, line 4; page 29, line 35 to page 30, line 5; Figure 1B
101, 102	Page 18, lines 35 - 36
103, 113	Page 11, lines 11-16; Page 9, line 36 to page 10, line 1; page 11, lines 11-16; page 12, lines 20-28; page 15, line 16; page 15, line 35 to page 16, line 4; Figure 1B; Figure 14
104	Page 10, line 2; page 12, lines 24-28; page 15, line 35 to page 16, line 4; page 29, line 35 to page 30, line 5; Figure 1B
105	Page 3, lines 35-36; page 11, lines 17-19
106	Page 3, lines 4-5; page 13, line 31 to page 14, line 5
107	Claim 16; page 4, line 25 (present amendment)
108	Page 33, lines 3-18; page 11, lines 11-16; Page 9, line 36 to page 10, line 1; page 11, lines 11-16; page 12, lines 20-28; page 15, line 16; page 15, line 35 to page 16, line 4; Figure 1B; Figure 14
109	Page 31, lines 32-33; page 33, lines 19-21
110	page 30, lines 24-25
111	page 30, lines 29-31
112	Page 3, lines 14-15; page 25, lines 8-16; page 30, lines 32-34

Support for the new paragraph at page 3, line 28, is provided by claim 16 as originally filed, with the exception that the new paragraph recites SEQ ID NO:29 instead of SEQ ID NO:30. As discussed in the Preliminary Amendment of October 21, 2002, SEQ ID NO:30 was erroneously designated as human Nogo A; the sequence of human Nogo A is provided in SEQ ID NO:29. At page 15, lines 13-16, it is stated that the rat Nogo amino acid sequence shown in Figure 2a is aligned with the human Nogo sequence shown in Figure 13. Figure 13 shows the alignment between rat and human Nogo proteins--the bottom rows of the alignment correspond to the sequence of Figure 2, *i.e.*, rat Nogo; the top rows represent human Nogo protein (by process of elimination). A comparison between the sequences in Figures 2a and 13 and the sequences in the Sequence Listing reveals that SEQ ID NO:29 corresponds to the sequence shown in Figure 13; therefore, SEQ ID NO:29 represents human Nogo protein. It will be clear to one of skill in the art that SEQ ID NO:30 is the sequence shown in Figure 2; and therefore, SEQ ID NO:30 represents rat Nogo protein. The new paragraph differs from claim 16 as filed in that the new paragraph recites the correct sequence identifiers. Thus, no new matter has been added.

The specification has further been amended to overcome the objections to the drawings and to the disclosure, as set forth in the Office Action of February 19, 2004, as discussed below.

1. THE OBJECTION TO THE DRAWINGS SHOULD BE WITHDRAWN

The drawings have been objected to because they include reference signs that were not mentioned in the description. In particular, Figure 2 contains "2A1-2A4," Figure 12 contains "12A-12D," Figure 13 contains "13A-13B," and Figure 14 contains "14A-14C." In response, Applicants have amended the Description of the Figures in the specification to recite the reference signs of the figures. These amendments correct clerical errors and do not introduce new matter. Applicants respectfully request that the objection be withdrawn in view of the present amendments.

2. THE OBJECTION TO THE DISCLOSURE SHOULD BE WITHDRAWN

The disclosure has been objected to because it contains embedded hyperlinks. Applicants have deleted the hyperlinks from the specification and have replaced the hyperlinks with a description of the web sites to which the hyperlinks were directed. In view

of the present amendments, Applicants respectfully request that the objection to the disclosure be withdrawn.

3. THE REJECTION UNDER 35 USC § 112 BASED ON NON-ENABLEMENT SHOULD BE WITHDRAWN

Claims 1-13, 16-18, 20, and 21 are rejected under 35 U.S.C. § 1.112, first paragraph, because the specification allegedly does not provide enabling support for any as of yet unspecified Nogo proteins. In particular, the Examiner contends that the specification fails to provide any guidance for the isolation and characterization of a genus of proteins commensurate in scope with the claims as filed. Applicants respectfully point out that the claims as filed have been replaced by new claims 98-113. The new claims recite SEQ IDs and specific ranges of amino acid sequence and sequence homologies. Applicants assert that the specification provides sufficient support for the isolation of proteins commensurate in scope with the new claims. Specifically, Applicants point out that the specification provides a representative number of species within the genus of the claimed proteins, namely rat, human and bovine Nogo sequences.

THE LEGAL STANDARD FOR ENABLEMENT

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

The law also does not require the scope of enablement provided by the specification to mirror precisely the scope of protection sought by the claims. *See In re Fisher*, 166 USPQ 18, 24 (C.C.P.A. 1970); *see also In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993). To be enabled, all the law requires is that the scope of enablement provided by the specification bear a "reasonable correlation" to the scope of the claims. *Id* Thus, to support a non-enablement rejection, the Examiner must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate the teaching in the specification across the entire scope of the claims. *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995).

In addition, the Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of non-enablement. *In re Marzocchi*, 169 USPQ 367, 369 (C.C.P.A. 1971); MPEP § 2164.02. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *Id.*

THE CLAIMS ARE ENABLED BY THE INSTANT SPECIFICATION

The gravamen of the Examiner's rejection is that the art of isolating and characterizing new genes based on sequence homology is unpredictable and that any experimentation that is required to isolate and characterize the claimed proteins is undue.

Applicants respectfully disagree and point out that enabling support for the claimed compositions is provided throughout the specification in form of guidance on how proteins with the recited amino acid sequence and sequence homologies can be isolated. For example, Section 5.1, beginning at page 12, line 12, describes how genes that encode proteins of certain degrees of sequence homologies can be isolated. In particular, at page 13, line 14 to page 14, line 18, support is provided for hybridization conditions that can be used to obtain nucleic acids that encode the proteins of varying degrees of amino acid sequence homologies. Further, at page 16, lines 5 to 33, the specification enumerates software programs that can be used by the skilled artisan to identify the claimed proteins or nucleic acids that encode such claimed protein in a database. The specification teaches at page 17, line 15, that about 180 amino acids at the carboxy-terminus of Nogo A (SEQ ID NO:2) are conserved among different species. The skilled artisan knows that regions of a gene that encode a conserved

domain can be used to identify homologs of the gene in other species. At page 18, lines 5-10, the specification describes how expression libraries can be used to identify Nogo homologs. Antibodies that can be used to identify homologs of Nogo in an expression library are also provided by the present specification, see, *e.g.*, at page 28, line 1 to page 29, line 32. At page 18, lines 11-31, the specification describes how polymerase chain reaction ("PCR") can be used to identify proteins that fall within the scope of the claimed proteins. The skilled artisan would know that primers for the PCR reaction can be designed based on the nucleic acid sequence that encodes a conserved region of the protein, such as the conserved carboxy-terminal 180 amino acids of Nogo A. Strategies for cloning genes encoding the claimed proteins from genomic DNA are described, *e.g.*, at page 19, lines 11-28.

Moreover, the specification provides several working examples describing the isolation and characterization of the claimed proteins using different methods. In Example 6, the isolation of a cDNA encoding a Nogo protein is described. Briefly, a portion of the biochemically purified bovine Nogo protein was microsequenced and the amino acid sequence was used to design primers that were used to identify cDNAs from a bovine cDNA library. DNA from the clone that was isolated from the bovine cDNA library was subsequently used to identify a rat cDNA. Thus, the isolation of the bovine and rat Nogo genes provides a working example for the use of PCR and nucleic acid hybridization in obtaining Nogo genes from different species of animals. The identification of human Nogo is described in section 7, page 69, lines 1-20. The human Nogo sequence was identified using the rat sequence as a frame of reference for the alignment and assembly of human EST sequences. The identification of human Nogo provides a working example for using information in sequence databases to obtain Nogo genes. Thus, the specification provides not only an adequate number of working examples for the isolation and identification of different Nogo genes, the specification also provides a number of different methods that were used for the isolation and identification of the different Nogo genes.

Because of the conserved structure and function of Nogo across species, the isolation and/or identification of Nogo genes in other species is not unpredictable. The specification shows that the amino acid sequences of human and rat Nogo A are 91% identical to each other. Further, the cross-species experiments described in the specification also demonstrate the conservation of Nogo structure and function across species. For example, at page 65, lines 15-16, it is described that bovine Nogo can inhibit the neurite outgrowth of NIH 3T3

cells, a mouse cell line. This concept is also supported by the observation that antibodies against the bovine Nogo protein promote neurite outgrowth of chicken dorsal root ganglia (see specification at page 65, lines 16-20).

Regions of the Nogo protein that confer inhibitory activity, *e.g.*, regions that inhibit spreading of fibroblasts, are identified, as described in section 6.2.7 of the specification at page 67, line 18, to page 68, line 33. The skilled artisan would know that if the sequence of the major inhibitory domain (specification at page 68, lines 28-30) is conserved, the inhibitory activity will also very likely be conserved. It is commonly known to the skilled artisan that the amino acid sequence of a functional region of a protein is very likely conserved across species if the function of that region is maintained in different homologs of the protein. Thus, the skilled artisan would know to use the nucleic acid sequence that encodes the major inhibitory domain of Nogo to isolate homologs of Nogo using cDNA library screens or PCR, or to identify sequences of Nogo homologs using electronic databases.

The Examiner cites Wells, 1990, Biochemistry 29:8509-8517 ("Wells") and Ngo *et al.*, 1995, In: The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14, pp.492-495 ("Ngo") to support the notion that in certain regions of a protein, mutations can have significant effects on protein structure and thereby on its function. Because Applicants have not taught where such regions are in the Nogo protein, the Examiner argues further, the specification lacks sufficient guidance to enable the skilled artisan to identify without undue experimentation the regions of the Nogo protein that are tolerant to change. Applicants respectfully disagree because regions of the Nogo protein that confer inhibitory activity, *e.g.*, regions that inhibit spreading of fibroblasts, are identified, as described in section 6.2.7 of the specification at page 67, line 18, to page 68, line 33. Thus, the skilled artisan would expect that the regions that are necessary for the inhibitory activity of Nogo protein would be conserved. Further, Applicants provide the amino acid sequences of rat, human and bovine Nogo, a representative number of species of mammalian Nogo proteins. Using knowledge common in the art, the skilled artisan would know how to align those sequences and identify non-conserved amino acid residues, thereby determining which amino acid residues should tolerate change without impairing the function of Nogo. An illustrative alignment between rat Nogo and human Nogo is shown in Figure 13 of the specification and shows the positions of conserved amino acid residues.

The Examiner also argues that even if the active site were identified, mutations in surrounding regions of the protein may still affect the protein's structure and thus its function. In Example 6.2.7 of the specification at page 67, Applicants have shown that the activity of the major inhibitory domain of Nogo (see the specification at page 68, lines 28-30) is maintained even if different parts of Nogo (other than the major inhibitory domain) are deleted (see Figure 18 and Table 2 at page 68). Thus, the major inhibitory domain of the Nogo protein can function independently of some other regions in Nogo.

The Examiner further cites Bork, 2000, Genome Research 10:398-400 ("Bork") and Skolnick and Fetrow, 2000, Trends in Biotechnology 18(1):34-39 ("Skolnick") to support the notion that a protein's function cannot be predicted from its structure alone. At the outset, Applicants respectfully point out that prediction of protein function based on primary structure, *i.e.*, amino acid sequence, has to be distinguished from protein function prediction based on three-dimensional structure. Both references, Bork and Skolnick, teach that sequence-based approaches to function prediction are well-established techniques. The presently claimed proteins are identified by virtue of their amino acid sequence homologies to, among others, SEQ ID NO:2 and not by virtue of their three-dimensional structures.

Skolnick states at page 34, right column, second full paragraph, that the sequence-to-function approach is a robust field. Even though Skolnick states at page 35, 2nd paragraph, 2nd sentence that "knowing a protein's three-dimensional structure is insufficient to determine its function," Skolnick does not teach that function cannot be predicted from primary structure, *i.e.*, amino acid sequence. Rather, Skolnick teaches that sequence-to-function approaches are powerful, although with limitations.

Bork is primarily concerned with the error margins of computational methods which limit the accuracy of function prediction to somewhere from 50% for the prediction of human promoters to up to 90% for the prediction of functional features based on homology (see Table 1 at page 399). Bork merely teaches that such limitations have to kept in mind when processing the results (see bottom of column 1 on page 400 of Bork) and concludes at page 400, middle column, first full paragraph, third sentence, that "there is still no doubt that sequence analysis is extremely powerful."

The Examiner further cites Doerks *et al.*, 1998, Trends in Genetics 14: 248-250 ("Doerks"), Smith and Zhang, 1997, Nature Biotechnology 15:1222-1223 ("Smith"), Brenner, 1999, Trends in Genetics 15:132-133 ("Brenner"), and Bork and Bairoch, 1996, Trends in

Genetics 12:425-427 ("Bairoch") to support the notion that function cannot be predicted from structure alone. For clarification, Applicants would like to point out that Doerks, Smith, Brenner, and Bairoch are primarily concerned with functional annotation using sequences in gene sequence databases, and not with the three-dimensional structure of proteins.

Doerks is concerned with the use of software robots to transfer functional features from annotated proteins in sequence database to query sequences, and recommends more precise database annotation by a skilled artisan. Smith, Brenner, and Bairoch also discuss the process of large-scale automated sequence annotation and the maintenance of data quality in the sequence databases. These references reiterate that the prediction of function based on sequence information in a database, although reliable for the most part, is not perfect, and this is in part due to the incomplete or erroneous annotations in sequence databases. The references focus on the reliability of using sequence database to assign one or more previously unrecognized functions to an anonymous segment of amino acid sequence. However, Applicants submit that these observations are not relevant to the present issue since the function of Nogo is known. Moreover, these observations made in the references are generally applicable to the sequence databases at large and not in particular to Nogo proteins. Applicants have taught which regions in the Nogo proteins are of functional significance; the skilled artisan would therefore know which regions should be conserved in order to preserve the function of Nogo. The present specification also teaches the primary structure of rat, human and bovine Nogo proteins. The skilled artisan knows how to align those sequences and identify conserved regions in those proteins. The sequence of the conserved regions can then be used (i) to make nucleic acid probes to clone other Nogo sequences or (ii) to identify other Nogo proteins in sequence databases.

Thus, in summary, Applicants submit that these references reinforce the notion that sequence information can be used to predict function and given the disclosure in the specification of functional assays (see Section 6.2.7 on pages 67-68 of the specification) and the plurality of sequence information from multiple species, only routine experimentation is required to enable the claimed invention. Applicants respectfully request that the rejection of claims 1-13, 16-18, 20, and 21 are rejected under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 14, 15, 19, 50, 51 and 54 are rejected under 35 U.S.C. § 1.112, first paragraph, because the specification allegedly does not provide enabling support for any as of yet

unspecified Nogo proteins. The Examiner supports the enablement rejection of claims 14, 15, 19, 50, 51 and 54 with substantially the same arguments that were used to support the enablement rejection of claims 1-13, 16-18, 20 and 21. Applicants respectfully point out that new claims 98 to 114 replace the previously pending claims and that the discussion above applies to all new claims.

4. THE REJECTION UNDER 35 U.S.C. § 112 BASED ON LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 1, 2, 5, 8-21, 50, 51, and 54 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to meet the written description requirement. The gravamen of the Examiner's rejection is that the specification allegedly does not provide sufficient distinguishing identifying characteristics of the claimed genus. In response, Applicants point out that the new claims recite actual sequences and sequence homologies as limitations, which are fully described in the specification. Further, Applicants point out that they have taught in the specification as originally filed a representative number of working examples within the scope of the claimed genus.

THE LEGAL STANDARD

The test for sufficiency of written description is whether the disclosure of the application 'reasonably conveys to the artisan that the inventor had possession' of the claimed subject matter. *In re Kaslow*, 707 F.2d 1366, 1375, 217 U.S.P.Q. (BNA) 1089, 1096 (Fed. Cir. 1983); accord *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563; *see also*, *Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575, 227 U.S.P.Q. (BNA) 177, 179 (Fed. Cir. 1985). The Court of Appeals for the Federal Circuit has repeatedly considered the written description requirement and consistently found that exacting detail is not necessary to meet the requirement:

> If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if [not] every nuance of the claims is explicitly described in the specification, the adequate written description requirement is met.
> *In re Alton*, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, p. 1099-1111), specifies that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a) above), reduction to drawings (see (1) (b) above), or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see (1)(c), above). *Id.* at p. 1106, column 3, *l.* 13-29.

Where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced.

Furthermore, in accordance with the Guidelines, what is conventional or well known to one of skill in the art need not be disclosed in detail, and, where the level of knowledge and skill in the art is high, a written description question should not be raised.

THE INSTANT SPECIFICATION PROVIDES SUFFICIENT WRITTEN DESCRIPTION FOR THE CLAIMS

The Examiner contends that the claims do not require that the proteins have a particular conserved structure or function. In response, Applicants point out that the new claims recite specific sequences or required minimum sequence homologies to specific sequences. The recited sequence homologies describe and limit the structure of the claimed proteins. Thus, the proteins of the new claims have a defined structure.

The Examiner contends that the specification is silent on the structure of Nogo B. Applicants respectfully disagree. The specification teaches that Nogo B is an alternative splice form of Nogo A (see the specification at page 5, lines 7-11, page 12, lines 22-23, and Figure 1B). The positions of the splice junctions are shown, *e.g.*, in Figure 1B, and described at page 12, lines 20-23. However, the new claims recite sequences or homologies to certain sequences, instead of gene names.

Claim 12 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to meet the written description requirement. In particular, the Examiner argues that the specification must provide sufficient distinguishing identifying characteristics of the genus. Applicants assert that they have met this requirement by describing a genus of proteins that have a minimum sequence identity to at least one of several specified amino acid sequences and by providing a representative number of species within that genus, namely human, bovine and rat Nogo proteins. The isolation of a bovine Nogo cDNA is disclosed in Example 6 beginning at page 56. The bovine Nogo cDNA was subsequently used to identify a rat cDNA. The identification of human Nogo is described in section 7, page 69, lines 1-20.

Further, the Examiner cites *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (Bd. Pat. App. & Int. 1993); and *Amgen v. Chugai Pharmaceuticals Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991) to support the notion that the structure of the claimed compound is required. *Amgen* describes what is necessary for conception: "Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it." *Amgen*, at 1021. *Fiers* states that "one cannot describe what one has not conceived." *Fiers*, at 1606. The present specification, however, does provide the structure of the claimed chemical in the form of amino acid sequences of Nogo proteins. ("A gene is a chemical compound, albeit a complex one." *Amgen*, at 1021.)

Further, *Fiers* stands for the proposition that a method for isolating a DNA molecule is not sufficient to fulfill the written description requirement for that DNA molecule. In contrast to *Fiers*, however, Applicants teach the structures, *i.e.*, sequences, of several representative species of the claimed genus of sequences. *Fiers* is inapplicable to the present application because in *Fiers* not a single sequence was taught.

In *Fiddes*, only one species, bovine pituitary FGF, of the genus mammalian FGF was disclosed. In contrast to *Fiddes*, the present application provides several Nogo proteins and their amino acid sequences from different species.

The different Nogo proteins and their sequences that are disclosed in the application demonstrate that Applicants had possession of the claimed genus. The Nogo genes that were isolated and described are derived from different species that are not closely related. The isolated Nogo genes, *i.e.*, human, rat, and bovine Nogo, have different, yet homologous

sequences that all fall within the scope of, *e.g.*, claim 98. Thus, the disclosed proteins are representative of the claimed genus.

5. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, IS OBVIATED

Claims 13 and 18 were rejected under 35 USC § 112, second paragraph, as being indefinite. In particular, the Examiner contends that claims 12 and 18 are indefinite because they recite the term "hybridizable." According to applicable case law, the requirement of 35 U.S.C. § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. Standard Oil Co. v. American Cyanamide Co., 774 F.2d 448, 227 U.S.P.Q. 293 (C.A.F.C. 1985). The test of definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. Orthokinetic Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1 U.S.P.Q.2d 1081 (C.A.F.C. 1986).

Applicants respectfully point out that new claim 106, which corresponds to original claim 13, recites that the nucleic acid hybridizes under conditions of high stringency. Thus, the term "hybridizable" is no longer recited in the claim. Conditions of high stringency are described in the specification as originally filed at page 13, line 31 to page 14, line 5. Thus, one of skilled in art would understand the scope of the claims clearly and definitely.

The rejection under 35 USC § 112, second paragraph, is obviated.

6. THE REJECTION UNDER 35 USC § 102 SHOULD BE WITHDRAWN

Claims 1, 14, and 20 are rejected under 35 USC § 102(a) as allegedly anticipated by Spillmann *et al.*, 1998, Journal of Biological Chemistry 273(30):19283-19293; "Spillmann et al."). First, Applicants believe that it is likely that the new claims by virtue of the recited degrees of amino acid sequence homologies do not encompass the bovine Nogo protein described in Spillmann. However, solely to expedite prosecution, Applicants respectfully point out that Spillmann et al. is not prior art under 35 USC § 102(a).

35 USC § 102(a) requires that

> the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent (emphasis added).

In response, Applicants point out that Spillmann, which is co-authored by Prof. Dr. Martin E. Schwab, one of the inventors, and others, was published in July of 1998, which is

within one year of the effective filing date of the present application, *i.e.*, November 6, 1998, the filing date of U.S. Provisional Application No. 60/107,446 (the "'446 Application"), to which the present application claims benefit of priority. The present application is a national stage application under 35 U.S.C. § 371 of International Patent Application No. PCT/US99/26160 (the "'160 Application") filed November 5, 1999. The '160 Application claims benefit of priority of the '446 application under 35 U.S.C. § 119(e).

Support for the Nogo protein amino acid sequences can be found in the '446 Application, *e.g.*, in Figure 2 (nucleotide sequence and amino acid sequence of rat Nogo A), Figure 13 (alignment between human and rat Nogo A amino acid sequences), and Figure 14 (rat Nogo C). In particular, Applicants believe that written description and enabling support under Section 112 can be found in the '446 Application for the pending claims 98-109 and 112-113 as set forth in the chart below.

Claim	Support in the '446 Application
98	Page 11, lines 28-29; Figure 2; page 13, lines 15-21; page 18, lines 18-25; page 32, line 31 to page 33, line 2
99	Page 11, lines 28-29; Figure 13; page 13, lines 15-21; page 18, lines 18-25; page 32, line 31 to page 33, line 2
100	Page 11, lines 28-29; Figure 14; page 13, lines 22-28; page 18, lines 18-25; page 32, line 31 to page 33, line 2
101	Page 22, line 12
102	Page 22, line 12
103	Page 11, lines 28-29; Figure 2; Figure 13; Figure 14; page 13, lines 15-28; page 32, line 31 to page 33, line 2
104	Page 32, lines 6-14; Page 11, line 29; Figure 2; Figure 13; Figure 14; page 13, lines 15-28; page 32, line 31 to page 33, line 2
105	Page 11, lines 28-29
106	Page 15, lines 16-29
107	Page 32, line 31 to page 33, line 2; page 93, line 27 to page 94, line 5
108	Page 30, line 25 to page 31, line 4; Figure 2; Figure 13; Figure 14; page 13, lines 15-28; page 18, lines 18-25; page 32, line 31 to page 33, line 2
109	Page 94, lines 24-31
112	Page 3, line 29 to page 4, line 13

Claim	Support in the '446 Application
113	Page 32, lines 6-14; Page 11, line 29; Figure 13; page 13, lines 15-28; page 32, line 31 to page 33, line 2

Thus, Applicants believe that they are entitled to the benefit of priority of the '446 Application with respect to claims 98-109 and 112-113. With respect to these claims, Applicants therefore contend that Spillmann et al. is not available as prior art for any purpose under 35 U.S.C. § 102 or § 103. To support this contention, Applicants provide the accompanying Declaration Of Prof. Dr. Martin E. Schwab And Dr. Maio S. Chen Under 37 C.F.R. § 1.132 ("Declaration") as evidence that Spillmann et al. is Prof. Dr. Martin E. Schwab's own publication, which occurred less than one year prior to the effective filing date of the present application. *In re Katz*, 687 F.2d 450, 215 U.S.P.Q. 14 (C.C.P.A. 1982). In view of the facts set forth in the Declaration by the inventors, the Applicants request that the rejection under 35 U.S.C. § 102(a) be withdrawn with respect to claims 98-109 and 112-113.

With respect to claims 110 and 111, Applicants respectfully point out that these claims are not anticipated by Spillmann et al. Spillmann et al. does not teach or suggest the deletion mutants of rat and human Nogo proteins recited in claims 110 and 111, respectively. In particular, there is no disclosure in Spillmann et al. of a rat protein lacking the specified sequences, or of a human protein lacking the specified sequences.

Claims 1, 2, 3, 9, 10, 12, 13, 14, 15, 16, 18, 19, 20, and 21, are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Application No. 09/893,348 filed June 28, 2001 and published as US 2002/0072493 (the "'348 Application"). Applicants respectfully disagree, because the present application is a national stage application under 35 U.S.C. § 371 of the "'160 Application" (see above) filed November 5, 1999. Thus, Applicants are at least entitled to the priority date of the '160 Application of November 5, 1999 which predates the effective 102(e) date as a reference of June 28, 2001 of the '348 Application with regard to Nogo amino acid sequences of June 28, 2001, as discussed in detail below. Applicants wish to point out, however, that Applicants believe that they are entitled to the benefit of priority of the '446 Application with respect to pending claims 98-109 and 112-113.

LEGAL STANDARD

As set forth in *Lund v. Godtfredsen*, 376 F.2d 982, at 988 (C.C.P.A. 1967):

> It is also well settled that where a patent purports on its face to be a 'continuation-part' of a prior application, the continuation-in-part application is entitled to the filing date of the parent application as to all subject matter carried over into it from the parent application, whether for purposes of obtaining a patent or subsequently utilizing the patent disclosure as evidence to defeat another's right to a patent.

Further,

> [i]f, for example, the PTO wishes to utilize against an applicant a part of that patent disclosure found in an application filed earlier than the date of the application which became the patent, it must demonstrate that the earlier-filed application contains § § 120/112 support for the invention claimed in the reference patent. For if a patent *could not* theoretically have issued the day the application was filed, it is not entitled to be used against another as "secret prior art," the rationale of Milburn being inapplicable, as noted above. In other words, we will extend the "secret prior art" doctrine of Milburn and Hazeltine only as far as we are required to do so by the logic of those cases.

In re Wertheim and Mishkin, 209 U.S.P.Q. 554, at 564 (C.C.P.A. 1981).

Thus, in the case of a U.S. patent or a patent application publication that is a continuation-in-part, in order for its date as a 102(e) reference to be carried back to its priority application, the following conditions, *inter alia*, must be met: (i) the reference must contain a description of the subject matter that is applied against the application; and (ii) the subject matter that is applied against the application must have been carried over from that priority application whose filing date is used as the effective 102(e) date. See *In re Wertheim*, 191 U.S.P.Q. 90, at 99 (C.C.P.A. 1976); *In re Wertheim and Mishkin*, 209 U.S.P.Q. 554, at 561 (C.C.P.A. 1981).

THE '348 APPLICATION IS NOT 102(e) PRIOR ART WITH REGARD TO NOGO PROTEIN SEQUENCES

As explained above, Applicants' filing date is at least the filing date of the '160 Application of November 5, 1999. The '348 Application is a continuation-in-part application of U.S. Application No. 09/314,161 filed May 19, 1999 (the "'161 Application;" attached hereto as Exhibit 1), which in turn is a continuation-in-part application of U.S. Application No. 09/218,277 filed December 22, 1998, which was published as US 2003/0108528 (the "'277 Application;" attached as Exhibit 2). The '277 Application is a continuation-in-part

application of international patent application PCT/US98/14715 filed July 21, 1998 published as WO 99/34827 (the "'715 Application;" attached as Exhibit 3). Neither the '161 Application, the '277 Application, nor the '715 Application disclose any of the Nogo amino acid sequences that are disclosed in the '348 Application. Thus, the disclosure of Nogo amino acid sequences that are disclosed in the '348 Application was introduced in the application when the application was filed on June 28, 2001 and was not carried over from any of its priority applications.

Because neither the '161 Application, the '277 Application, nor the '715 Application disclose any of the Nogo amino acid sequences that are disclosed in the '348 Application, the effective 102(e) date as a reference of the '348 Application with regard to the disclosure of the Nogo amino acid sequences is the filing date of the '348 Application, *i.e.*, June 28, 2001. Thus, the effective 102(e) date of the '348 Application does not predate the filing date of the present application with regard to the pending claims.

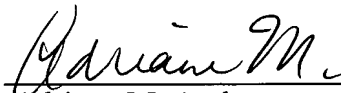
Accordingly, Applicants respectfully request that the rejections under 35 USC § 102 be withdrawn.

CONCLUSION

Applicants respectfully request that the present remarks and amendments be entered and made of record in the instant application. An allowance of the application is earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: August 19, 2004



32,605

Adriane M. Antler (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017
Telephone Number: 212-326-3939
Fax No.: 212-755-7306